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Title: The relation between spasticity and muscle behavior during the swing phase of gait in children with cerebral palsy

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Abstract: There is much debate about how spasticity contributes to the movement abnormalities seen in children with spastic cerebral palsy (CP). This study explored the relation between stretch reflex characteristics in passive muscles and markers of spasticity during gait. Twenty-four children with CP underwent 3D gait analysis at three walking velocity conditions (self-selected, faster and fastest). The gastrocnemius (GAS) and medial hamstrings (MEHs) were assessed at rest using an instrumented spasticity assessment that determined the stretch-reflex threshold, expressed in terms of muscle lengthening velocity. Muscle activation was quantified with root mean square electromyography (RMS-EMG) during passive muscle stretch and during the muscle lengthening periods in the swing phase of gait. Parameters from passive stretch were compared to those from gait analysis.
In about half the children, GAS peak muscle lengthening velocity during the swing phase of gait did not exceed its stretch reflex threshold. In contrast, in the MEHs the threshold was always exceeded. In the GAS, stretch reflex thresholds were positively correlated to peak muscle lengthening velocity during the swing phase of gait at the faster (r=0.46) and fastest (r=0.54) walking conditions. In the MEHs, a similar relation was found, but only at the faster walking condition (r=0.43). RMS-EMG during passive stretch showed moderate correlations to RMS-EMG during the swing phase of gait in the GAS (r=0.46-0.56) and good correlations in the MEHs (r=0.69-0.77) at all walking conditions. RMS-EMG during passive stretch showed no correlations to peak muscle lengthening velocity during gait.
We conclude that a reduced stretch reflex threshold in the GAS and MEHs constrains peak muscle lengthening velocity during gait in children with CP. With increasing walking velocity, this constraint is more marked in the GAS, but not in the MEHs. Hyper-activation of stretch reflexes during passive conditions is related to muscle activation during the swing phase of gait, but has a limited contribution to reduced muscle lengthening velocity during swing. Larger studies are required to confirm these results, and to investigate the contribution of other impairments such as passive stiffness and weakness to reduced muscle lengthening velocity.

1. INTRODUCTION

Cerebral palsy (CP) is the most prevailing cause of physical disability in children and is caused by an upper motor neuron (UMN) lesion that occurs in the developing brain, resulting in a set of primary impairments. Spasticity, one of the primary impairments, is reported to occur in approximately 85% of the children with CP (Cans, 2000). Its assessment and treatment are therefore central to the management of a child with CP.

Spasticity was defined by Lance as 'a velocity-dependent increase in tonic stretch reflex' (Lance, 1980). Following this description, spasticity can be assessed by applying a quick stretch to a passive muscle and evaluating the resistance to movement. The diagnosis of spasticity is confirmed by the presence of exaggerated muscle activation (measured for example using surface electromyography - sEMG) during this muscle stretch. This activation is caused by lack of central regulation resulting in a stretch reflex that has a pathologically lower activation threshold than unaffected muscles. While the definition of spasticity offered by Lance is relatively straightforward to measure in a passive muscle, it may not be applicable to voluntarily contracted muscle (Burridge et al., 2005).

Defining spasticity when a muscle is voluntarily contracted has proved more challenging (Biering-Sørensen, Nielsen, & Klinge, 2006; Pandyan et al., 2005). Unlike in passive assessments, muscle activation during voluntary activity cannot be solely attributed to a stretch reflex reaction. Nevertheless, in children with CP, spasticity during gait is thought to contribute to reduced ankle dorsiflexion and knee extension at terminal swing. These deficits are associated with reduced muscle lengthening velocities in the gastroc-soleus and hamstrings respectively, and can result in decreased step length and walking velocity (Delp, Arnold, Speers, & Moore, 1996).

Levin and Feldman suggested that persons with spasticity avoid or are unable to achieve high walking velocity due to the presence of lowered stretch reflex thresholds (Levin & Feldman, 1994). They defined this threshold as the *joint angle* or *joint angular velocity* at which sEMG significantly increased during stretch of a passive muscle (Levin & Feldman, 1994). However, especially in bi-articular muscles, such as the gastrocnemius and hamstrings, the study of the *muscle length* and *lengthening velocity* thresholds (estimated based on musculoskeletal modeling (Delp et al., 1990)) provide more direct information on the trigger of spasticity than joint angles and angular velocities.

Different approaches exist to assess the effect of spasticity and stretch reflex thresholds on muscle lengthening velocity. The first was introduced by Crenna in his concept of dynamic spasticity (Crenna, 1998). He highlighted that decreased muscle lengthening velocity in the gastrocnemius of children with spastic CP is coupled with higher muscle activation during the stance phase of gait (Crenna, 1998). Following this approach, a later study confirmed these results in the calf muscles of

children with CP (van der Krogt, Doorenbosch, Becher, & Harlaar, 2010), but during the swing rather than the stance phase.

The second approach is to compare the findings of spasticity during passive assessment to signs of spasticity during gait. However, studies that have followed such an approach have mostly relied on the clinical spasticity scales (Desloovere et al., 2006; van der Krogt, Doorenbosch, & Harlaar, 2009). Desloovere et al. (2006) for example, found no correlations between gastrocnemius and hamstrings Modified Ashworth scale (MAS) or Modified Tardieu scale (MTS) scores and maximum knee flexion velocity during swing in children with CP (Desloovere et al., 2006). Researchers that have used instrumented assessments reported that low stretch reflex thresholds in the hamstrings and rectus femoris were associated with reduced knee joint angular velocities during gait, especially at faster walking speeds (Damiano, Laws, Carmines, & Abel, 2006; Tuzson, Granata, & Abel, 2003). On the other hand, some studies have failed to confirm a relation between the presence of spasticity as measured during rest conditions and gait pathology (Ada, Vattanasilp, O'Dwyer, & Crosbie, 1998; Marsden, Ramdharry, Stevenson, & Thompson, 2012; Willerslev-Olsen, Andersen, Sinkjaer, & Nielsen, 2014). It has become clear that despite the vast amount of available research, there is still no consensus about the influence of spasticity on gait in children with CP. Nevertheless, spasticity reduction remains one of the main interventions used in children with spastic CP. This is an important issue that requires more research to resolve.

An instrumented assessment for measuring spasticity in resting muscles has recently been validated for use in the gastrocnemius and hamstrings of children with CP (Bar-On et al., 2012). The current study aimed to establish whether spasticity as assessed in the passive muscle using an Instrumented Spasticity Assessment (ISA) is related to gait features during the swing phase of gait in children with CP. Muscle lengthening velocity thresholds (mlvT) and EMG gain, as assessed with ISA, were compared to the peak muscle lengthening velocity (max mlv) and muscle activation during the swing phase of gait. In contrast to previous studies on this research topic, stretch reflex thresholds are expressed in terms of muscle lengthening rather than angular velocity. Additionally, we investigated whether children with different degrees of spasticity remain below or above their mlvT while walking at increasing velocities. The data analysis focused on the lateral gastrocnemius (GAS) and medial hamstrings (MEHs) and on sub-phases of swing during which the observed muscles lengthen. We hypothesized that muscles with higher spasticity (i.e. low mlvT and high EMG gain during the passive test) will exhibit increased muscle activation and reduced max mlv during these sub-phases of swing. We expected that these relations will be stronger than previous investigations that relied on clinical spasticity scales (Desloovere et al., 2006).

2. METHODS

2.1 Participants

The study involved a prospective cohort of participants recruited from the multidisciplinary CP-reference center at the University Hospital Pellenberg. Children aged 5-18 years were screened for inclusion. Exclusion criteria were the presence of ataxia or dystonia, severe muscle weakness (<2+ on the Manual Muscle Test (Hislop & Montgomery, 1995)), poor selectivity (Gage, 2009), bone deformities or contractures compromising the performance of pure single-plane passive ankle or knee movements, cognitive problems that could impede the measurements, previous lower limb orthopedic or neuro-surgery, or Botulinum Toxin-A injections in the past 6 months. Children's parents signed an informed consent for participation. The experimental protocol was approved by the university hospital's ethical committee (B32220072814).

2.2 Experimental protocols

2.2.1 Instrumented spasticity assessment (ISA)

All children were first tested by one trained assessor with ISA. The measurement setup for ISA for the GAS and MEHs is presented in Figure 1. Measurements were always performed on the most affected side. This was defined as the side with highest averaged MAS of the two muscles (Bohannon & Smith, 1987), or in case of symmetrical averaged MAS scores, the side with most severe averaged MTS R1 angle measured during a fast muscle stretch (Boyd & Graham, 1999). ISA for the MEHs and GAS have been previously described (Bar-On et al., 2012). Throughout the measurement procedure, sEMG data from GAS, MEHs, and their antagonists (tibialis anterior and rectus femoris, respectively) was collected using a telemetric Zerowire system (Cometa, Milan, IT) at a sample rate of 2000 Hz. sEMG electrodes were placed according to a standardized procedure (Hermens, Freriks, Disselhorst-Klug, & Rau, 2000). Antagonist activation was used to detect other tone problems (e.g. dystonia) or active assistance of the child during passive stretches.

An ISA measurement started with three repetitions of maximal voluntary contractions (MVCs) of the agonist and antagonist carried out with the subject in supine position. Subjects were then asked to remain relaxed while the movement of the distal limb segment with respect to the proximal was tracked using two inertial measurement units (IMUs: Analog Devices, ADIS16354) that recorded angular velocity and acceleration during ankle and knee joint position calibrations as described in (Bar-On et al., 2012). Muscle stretches were then manually applied by passively moving one joint at a time from a predefined starting position (while keeping the proximal, non-moving joints manually fixated) through the full range of motion (ROM). These stretches were performed at low, medium, and high velocities. For the current study, only movements at high velocity, representing a stretch

performed as fast as possible, were analyzed. These high velocity stretches were the most representative of the lengthening velocity during gait and were most likely to have been fast enough to evoke a stretch reflex response. Each stretch trial was repeated four times with an interval of 7 seconds rest between repetitions.

2.2.2 3D gait analysis

Prior to ISA, children underwent 3D gait analysis. Lower limb dimensions and body height were measured to enable an estimation of joint centers. Children walked on a 10 m walkway at three walking conditions: (1) self-selected (SS) comfortable speed, (2) faster and (3) as fast as possible without running (fastest). Temporospatial and kinematic measurements were collected using a VICON system with 8 to 15 infrared cameras (Nexus capturing system measuring at 100 Hz, with lower limb Plug-In-Gait marker set, VICON, Oxford Metrics, Oxford, UK). sEMG data was collected from the GAS and the MEHs using the same telemetric Zerowire system used during ISA. At least nine valid barefoot walking trials on the walkway were collected, representing three trials for each walking velocity condition. A valid trial was obtained when there was good marker visibility and an artefact-free sEMG signal.

2.3 Data analysis

ISA and the 3D gait analysis resulted in a set of outcome parameters based on sEMG and muscle length data. To justify and facilitate comparison, the outcome parameters from both assessments were analyzed in the same manner (see below) and expressed in the same units.

2.3.1 ISA

Data visualization and analyses were carried out using custom software implemented in MATLAB©. Joint angles were obtained after applying a Kalman smoother (Rauch, Tung, & Striebel, 1965) on the IMU data. By visualizing the data, stretch repetitions were excluded when passive stretches were performed at inconsistent velocities between different repetitions within a velocity trial (difference >20°/s) or when performed out of plane (see Supplement 1 in (Bar-On et al., 2012)). Passive stretches were also excluded in case of poor quality sEMG (low signal-to-noise ratio or obvious artefacts), and in case of antagonist activation. Starting from the joint angles, muscle lengths were calculated using OpenSim software (Delp et al., 2007). Individual segment lengths were scaled using kinematic data derived from a static trial measured during the 3D gait analysis. All muscle lengths were expressed as a percentage of the muscle length in the anatomical zero position. The muscle lengthening velocity (*mlv*, expressed in %/sec) was calculated using the derivative of the muscle

length. The average maximum mlv was calculated by averaging the values from four stretch repetitions at high velocity (*max mlv passive*).

Raw sEMG signals were filtered with a 6th order zero-phase Butterworth bandpass filter from 20 to 500 Hz. The root mean square envelope of the sEMG (RMS-EMG) was extracted by applying a low-pass 30 Hz 6th order zero-phase Butterworth filter on the squared signal. EMG onset was defined according to the method of Staude and Wolf (Staude & Wolf, 1999). This automatic onset detection method applies an approximated generalized likelihood principle by detecting statistically optimal changes throughout the signal (Staude & Wolf, 1999) and has been shown to perform significantly better compared to threshold based algorithms (Lee, Cholewicki, & Reeves, 2007)**.** Only muscles in which sEMG onset was detected during high velocity stretches were included in the analysis as this indicated the presence of spasticity. The muscle lengthening velocity threshold (*mlvT*, expressed in %/sec) was defined as the mlv at which EMG onset occurred during a high velocity stretch. Values from stretches at high velocity were averaged to calculate one overall mlvT per muscle.

EMG gain was quantified by calculating the average RMS-EMG during high velocity stretches in which EMG onset was detected. Average RMS-EMG was defined as the area underneath the RMS-EMG time curve divided by the duration of the time interval considered. This time interval started 200ms prior to the time corresponding to maximum angular velocity and ended at the time corresponding to 90% of the full ROM (Bar-On et al., 2012). This value was then normalized by expressing it as a percentage of the peak RMS-EMG value of the MVCs. These normalized values from stretches at high velocity were averaged to calculate one *RMS-EMG passive* value per muscle.

2.3.2 3D gait analysis

Kinematic data was based on the lower limb Plug-In-Gait model running in Nexus software (VICON, Oxford Metrics, Oxford, UK). Using the same software, two gait cycles per trial were identified by visually determining events of initial contact and toe off. Muscle lengths were calculated using the obtained kinematics and OpenSim software (Delp et al., 2007). Kinematic data derived from the static trial were used for scaling individual segment lengths. Similar as for ISA, all muscle lengths were expressed as a percentage of the corresponding muscle length in the anatomical position and the derivative of the muscle length was calculated to obtain the maximum lengthening velocity during swing (*max mlv swing*, expressed in %/sec). Visual quality control of all sEMG, kinematics, and muscle lengths was carried out in custom software implemented in MATLAB©.

Per walking condition, the average max mlv swing was calculated from the different trials. For each individual patient, these values were plotted per walking condition against percentage of the gait cycle. The corresponding average mlvT extracted from ISA was then plotted as a horizontal line on this mlv graph (Figure 2). This allowed for a visual comparison of how the muscles lengthened

during gait relative to their mlvT. The difference between max mlv swing and the average mlvT was calculated per muscle and per walking condition (*Diff mlv*, expressed in %/s).

RMS-EMG was derived from the raw sEMG signals as described above. Average RMS-EMG was calculated by dividing the RMS-EMG signal by the time phase during swing in which the muscle was lengthening. This value was then normalized by expressing it as a percentage of the peak RMS-EMG value of the MVCs carried out during ISA. Per walking condition, the average normalized RMS-EMG during the lengthening phase of swing was calculated from the different trials (*RMS-EMG swing*).

2.4 Statistics

The inter-session reliability and corresponding absolute measurement error of parameters from ISA were calculated from a cohort of 10 children with CP previously described (Bar-On et al., 2014). Descriptive statistics of all parameters (max mlv passive, mlvT, RMS-EMG passive, max mlv swing, diff mlv, and RMS-EMG swing) were calculated per muscle. The parameters from 3D gait analysis were defined at each walking condition. All parameter distributions were checked for normality using Kolmogorov–Smirnov test with $p > 0.1$ indicating a normal distribution. Statistical tests were chosen as appropriate to the distribution. Therefore, max mlv passive was compared to max mlv swing in each walking condition using either paired sample t-tests, or Wilcoxon Signed Rank Tests. Per muscle and per walking condition, either Pearson or Spearman rank correlation coefficients were calculated between parameters from ISA (mlvT and RMS-EMG passive) and parameters from 3D gait analysis (max mlv swing and RMS-EMG swing). Additionally correlations were sought between the RMS-EMG parameters from both conditions and diff mlv. Correlations coefficients were interpreted according to (Altman, 1999) and statistical significance was set to $p<0.05$. All statistical analyses were carried out in SPSS (IBM Statistics, Version 22).

3. RESULTS

Twenty-four children with CP participated in the study. One GAS measurement was excluded due to bad quality sEMG data during ISA. In another GAS, there was no EMG onset during high velocity passive stretches. Therefore, in total, 22 GAS and 24 MEHs muscles were analyzed (Table 1). Due to practical considerations, for three subjects, ISA was carried out prior to, rather than following the 3D gait analysis. The results from these subjects did not differ from the rest.

xxx insert table 1 here xxx

ICC values of the parameters collected during ISA ranged from good to excellent (ICC 0.78-0.93). These results, together with the standard error of measurement per parameter can be found in supplementary material 1. Descriptive parameters from ISA and from the 3D gait analysis can be

found in Table 2. The majority of parameters were not normally distributed. Therefore, only non-parametric statics were carried out. Figure 3 shows the group average max mlv values from ISA, during gait, and the group average mlvT. In GAS, average max mlv passive (32.2 ± 7.0 %/sec, corresponding to an ankle angular velocity of 173.5 ± 35.1 °/s) significantly differed from max mlv swing at the SS (25.2 ± 7.7 %/sec) and faster (26.5 ± 8.1 %/sec) walking conditions (p=0.009, and p=0.005, respectively). In the MEHs, average max mlv passive (50.2 ± 9.6 %/sec, corresponding to a knee angular velocity of 280.8 ± 45.9 °/s) significantly differed from max mlv swing at the faster (66.6 ± 19.2 %/sec) and fastest (73.4 ± 20.8 %/sec) walking conditions (p=0.004, and p=0.001, respectively). In GAS, negative group median diff mlv values indicated that max mlv swing was generally lower than the mlvT. In MEHs, positive group median diff mlv values indicated the opposite. In GAS, diff mlv decreased with increasing walking velocity, while in the MEHs, it increased.

Individual results indicated that for GAS, max mlv swing exceeded the mlvT in 7 of the 22 cases at the SS walking condition, in 9 cases at faster, and in 11 cases at the fastest walking condition. For the MEHs, max mlv swing was always higher than the mlvT, except in three children at the SS walking condition where it was lower.

In both muscles, RMS-EMG swing increased with increasing walking velocity. For GAS, RMS-EMG passive was about 23% of RMS-EMG swing and in the MEHs, this value was about 30%.

xxx Insert table 2 here xxx

Correlation coefficients between parameters from ISA and from 3D gait analysis are shown per muscle and per walking condition in Table 3. Figure 4 shows scatter plots between selected parameters from ISA and the gait parameters. In both muscles at all walking conditions, average RMS-EMG passive showed moderate to good positive correlations with average RMS-EMG swing (r=0.46-0.77, p<0.05). These latter correlations increased from SS to the faster walking condition, but decreased at the fastest walking condition (see Figure 4). In GAS, mlvT had moderate positive correlations to max mlv swing at the faster and fastest walking conditions (r=0.46, and r=0.54, respectively, p<0.05). In the MEHs mlvT max had a moderate positive correlation to mlv swing while walking at the faster walking condition (r=0.43, p<0.05).

xxx insert table 3 here xxx

xxx insert figure 4 here xxx

4. DISCUSSION

The aim of this study was to investigated the relationship between spasticity parameters at rest and markers of spasticity during the swing phase of gait in the GAS and MEHs of children with spastic CP. As expected, overall, the correlation coefficients found were higher than those of a previous study in which spasticity scores derived from the MAS and MTS were correlated to parameters from 3D gait analysis (Desloovere et al., 2006). This may be explained by the use of an instrumented assessment in the current study as well as the selection of specific gait features during the swing phase that highlight spasticity.

In the current study, spasticity at rest was assessed with an instrumented assessment allowing for a quantitative evaluation of the threshold (the mlvT) and gain (RMS-EMG passive) of the stretch reflex. Muscle lengthening and corresponding EMG were studied during the swing phase of gait at three incremental walking velocities. During the swing phase of gait, active foot dorsiflexion and knee extension are expected to induce stretch reflex activity in the GAS and MEHs, respectively. In subjects with impaired supraspinal control, lack of inhibition of this activity is thought to contribute to the prevention of adequate foot placement at initial contact (Dietz, 2002). However, there is no consensus on whether spasticity as assessed at rest reflects the activation of stretch reflexes during gait.

4.1 Correlation of mlvT and RMS-EMG passive to max mlv during the swing phase of gait

We have found moderate positive associations between the mlvT and the max mlv at the faster walking condition (both muscles), and at the fastest condition (GAS) indicating that the presence of a low spastic threshold may affect the ability of these muscles to lengthen during swing. On the other hand, RMS-EMG measured during passive stretch was not correlated to the max mlv achieved during this phase of gait.

At rest, spastic muscles exhibit reduced presynaptic and reciprocal inhibition, and an increased resting membrane potential, resulting in hyper active stretch reflexes (Dietz & Sinkjaer, 2007). When spastic muscles are activated, in addition to decreased spinal inhibitory mechanisms there is a lack of supraspinal modulation and a lack of long-latency reflexes (Sinkjaer, Andersen, Nielsen, & Hansen, 1999). It is this absence of long-latency reflexes that may help explain why RMS-EMG passive was not related to max mlv swing.

In a recent study by Willerslev-Olsen et al. (2014), calf stretch reflexes were evoked by mechanically perturbing the soleus length during the swing phase of gait in children with CP and typically developing (TD) children. The authors showed that short-latency stretch reflexes in the soleus were exaggerated at the end of swing in children with CP. However, due to the absence of

subsequent long-latency stretch reflexes, the overall sEMG measured in the soleus was similar to that of TD children. They concluded that pathological muscle activation might not contribute to altered ankle kinematics during swing in children with CP (Willerslev-Olsen et al., 2014).

Similarly, in the GAS of subjects post-stroke, Ada et al. (1998) found exaggerated reflex gain in rest condition, but lower reflex gain when the muscles were perturbed during active motions that simulated walking (Ada et al., 1998). In accordance, in the current study, the amount of RMS-EMG measured at rest was only around 30% of the amount measured during the swing phase of gait. Any reflex activation during gait may not have been enough to contribute towards a change in muscle length.

On the other hand, in the current study, low mlvT was found to be positively correlated to reduced max mlv during the swing phase of gait. Previous studies have also shown that low stretch reflex thresholds are related to motor impairment. For example, low spastic thresholds in the hamstrings were found to limit knee angular velocity during gait (Damiano et al., 2006; Tuzson et al., 2003). The current study confirms these findings and adds to the available literature by studying muscle lengthening velocity instead of joint angular velocity.

To the best of our knowledge, no other study has reported on the relations between mlvT defined by passive assessment and max mlv during swing in the GAS. However, previous research has shown that in contrast to typically developed subjects, H-reflexes and short latency stretch reflexes are not modulated in the GAS during the stance phase of gait (Dietz, 2002). This decreased modulation results in an abnormal appearance of short-latency reflexes during the swing phase of gait which can interfere with walking ability (Ada et al., 1998; Sinkjaer et al., 1999; Sinkjaer & Magnussen, 1994; Willerslev-Olsen et al., 2014). Similar results have been reported in the upper limbs of subjects post-stroke. In an elegant study by Musampa et al. (2007), joint angle stretch reflex thresholds assessed at rest were positively correlated to the positions at which muscles were activated when moved voluntarily. In addition, these relations depended on the configurations of multiple joints acting on a muscle. These findings confirm that the motor impairment is related to a lack of stretch reflex regulation and that this regulation is muscle-length dependent (Musampa et al., 2007).

4.2 Correlation between RMS-EMG passive and RMS-EMG during the swing phase of gait

In both muscles, RMS-EMG passive was positively correlated to muscle activation during the lengthening phase of swing. Hyper-activation of the stretch reflex during passive assessment thus seems related to increased muscle activation of GAS and MEHs in the swing phase of gait. An additional finding of the current study was that, in both muscles, these latter correlations slightly decreased with increasing walking speed. In a previous study we have shown that, in comparison to

typically developing (TD) children, EMG activation at the end of the swing phase in children with CP, is only higher at the self-selected walking velocity. With increasing walking velocity, TD children produce more muscle activation than CP children (Van Campenhout et al., 2014). Therefore, at the fastest walking condition increased activation may be better explained by the greater importance of other motor system adjustments involved in increasing walking velocity, such as co-contraction (Nielsen, Petersen, Crone, & Sinkjaer, 2005), muscle strength (Schwartz, Rozumalski, & Trost, 2008), and a more demanding control of balance.

4.3 Muscle-specific modulation

Some differences between the two studied muscles were noticed. First, in the GAS, increased walking velocity strengthened the effect of reduced stretch reflex modulation whereas in the MEHs it lowered it. Second, max mlv swing in the GAS generally did not exceed the mlvT, while in the MEHs max mlv swing nearly always surpassed mlvT. Third, the median mlvT occurred at 90% of max mlv passive for the GAS, while this already occurred at 60% for the MEHs. These results could indicate that the sensitivity of the reflex threshold to muscle lengthening velocity is muscle-specific. Recent findings indeed showed low velocity-dependent muscle activation for the MEHs during passive stretch, and high velocity-dependent muscle activation for the GAS (Bar-On, Aertbeliën, Molenaers, & Desloovere, 2014). Another possible explanation for these differences between muscles may be attributed to the starting muscle length during ISA. In both muscles, passive stretch was initiated from a longer muscle length because of the positioning of the proximal joints during testing (knee extension for the GAS test and 90° hip flexion for the MEH test). The GAS is reported to be less sensitive when stretched from initially longer lengths (Meinders, Price, Lehmann, & Questad, 1996), whilst the opposite appears true for the hamstrings (Sheean, 2008). More effort is required to replicate the exact muscle lengthening properties at rest and during walking before further conclusions can be drawn.

4.4 Study limitations

Some study limitations must be recognized. Firstly, different joint kinematics from ISA and from 3D gait analysis were used as input to derive the muscle lengths in OpenSim (Delp et al., 2007). For ISA, kinematics were calculated using data from the IMUs which were dynamically calibrated to the anatomical planes during measurement. On the other hand, the kinematics derived during 3D gait analysis were calculated using OpenSim (Delp et al., 1990). In the latter, the marker configuration was directly connected to the underlying anatomy by placing the markers on anatomical reference points. In an unpublished pilot study, comparing ISA with 3D kinematic data collected using Vicon

(Vicon, Oxford Metrics Group, UK), differences of 1-5˚ were found. These small differences ensured that the application of the model using both modalities was conceptually similar.

For both the passive and gait conditions, the generic model provided in OpenSim (Delp et al., 1990) was used to derive muscle lengths. Although in the current paper, we refer to muscle lengths, the model applied estimates muscle-tendon lengths. Furthermore, no adaptations were made to the model to reflect pediatric or pathological muscle morphology. Future developments should incorporate information from imaging to individualize musculoskeletal models.

Due to practical reasons, in a few cases, ISA was carried out before the gait analysis. Despite not finding significant differences between the results of these subjects and the rest, stretch reflex excitability may be influenced by muscle fatigue (Jobin & Levin, 2000). More investigations that assess the effect of fatigue on mlvT should be undertaken.

Lastly, the included subjects varied widely in age and anatomical distribution of their impairments. Both spasticity and gait patterns are known to vary with age (Hägglund & Wagner, 2008; Johnson, Damiano, & Abel, 1997), however the limited sample size of the current study did not permit for explorations into the effect of age.

4.5 Future directions and conclusions

It is worthwhile to investigate the effect of spasticity on other lower limb muscles. Spasticity in the rectus femoris has been associated with reduced maximum lengthening velocity (Jonkers, Stewart, Desloovere, Molenaers, & Spaepen, 2006) and reduced knee angular velocity (Tuzson et al., 2003). However, the precise contribution of rectus femoris spasticity to gait abnormalities, such as stiff-knee gait, is still uncertain (Reinbolt, Fox, Arnold, Ounpuu, & Delp, 2008).

Future work should also evaluate the impact of muscle *length* thresholds on gait features. Several studies have reported tonic muscle activation during very slow passive muscle stretch (Bar-On et al., 2014; Thilmann, Fellows, & Garms, 1991; van den Noort, Scholtes, & Harlaar, 2009). Low-velocity threshold activation is thought to be associated with muscle stiffness (Gracies, 2005). Thus, stiffer muscles may be sensitive to increasing length as well as lengthening velocity. Studying the impact of length thresholds on gait features may lend more insight on whether activation thresholds are regulated differently among different muscles with different mechanical properties.

Previous authors have shown that passive stiffness of the GAS and weakness of the tibialis anterior may be better predictors of limited GAS lengthening in swing than spasticity (Willerslev-Olsen et al., 2014). Limited MEH lengthening in swing could be explained by stiffness (Marsden et al., 2012), lack of balance, and the activation necessary to decelerate knee extension (Jonkers et al., 2006). Further research that adequately quantifies the amount of muscle strength and stiffness

should be carried out to further unravel the contributions of the major impairments to pathological gait.

In conclusion, reduced mlvTs were found to constrain max mlv in the GAS and MEHs during the lengthening phases of swing in children with CP. With increasing walking velocity, this constraint was more marked in the GAS, but not in the MEHs. Hyper-activation of stretch reflexes during passive conditions was related to muscle activation during the swing phase of gait, but may have only a limited contribution in causing reduced mlv during swing in children with CP. Larger studies are required to confirm these results, to investigate the effect of spasticity treatment on the mlvT, and to quantify the contribution of other impairments such as passive stiffness and weakness to reduced muscle lengthening velocity.

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Figure captions

Figure 1. Instrumented spasticity assessment starting positions, direction of stretch (curved arrow), and instrumentation for **(A)** the lateral gastrocnemius (GAS) and **(B)** the medial hamstrings (MEHs). Overview of the test instrumentation: (1) inertial measurement units measured joint angle characteristics; (2) surface electromyography measured muscle activity of the agonistic and antagonistic muscle groups; (3) a 6 degrees of freedom force sensor attached to a foot orthosis (GAS) or a shank orthosis on the posterior aspect of the lower leg (MEHs) was used to measure torque; (4) support frame for the lower leg.

Figure 2. Example of average muscle lengthening velocity (mlv) in **(A)** the gastrocnemius (GAS) and **(B)** the medial hamstrings (MEHs) from different trials per walking condition [self-selected walking (red line), faster (green line), and fastest (blue line)] plotted against percentage gait cycle in a child with CP. Muscle lengthening velocities are expressed as a percentage of the muscle length at anatomical position. Shaded areas, outlined by vertical colored lines, represent periods during the swing phase when the muscle is lengthening in each walking condition. The straight horizontal gray line is the average muscle lengthening velocity threshold and its standard deviation (dotted gray lines) defined during high velocity passive muscle stretch.

Figure 3. The stretch reflex threshold (mlvT) and the average maximum muscle lengthening velocities during the high velocity passive stretches (max mlv passive) and during the swing phase (max mlv swing) at three walking conditions (SS, Faster, Fastest) in **(A)** the lateral gastrocnemius (GAS) and **(B)** the medial hamstrings (MEHs). *Significant differences between max mlv passive and max mlv swing.

Figure 4 Scatter plots between parameters from the passive assessment and gait parameters for GAS **(A, B)** and MEHs **(C, D)** with significant Spearmen linear correlation trendlines. **(A, C)** Maximum lengthening velocity in swing (max mlv swing) at self-selected (SS), faster, and fastest walking conditions versus the muscle lengthening velocity threshold (mlvT) **(B, D)** Root mean square electromyography during passive stretch (RMS-EMG passive) versus RMS-EMG during the lengthening phase of swing (RMS-EMG swing).

Figure 1

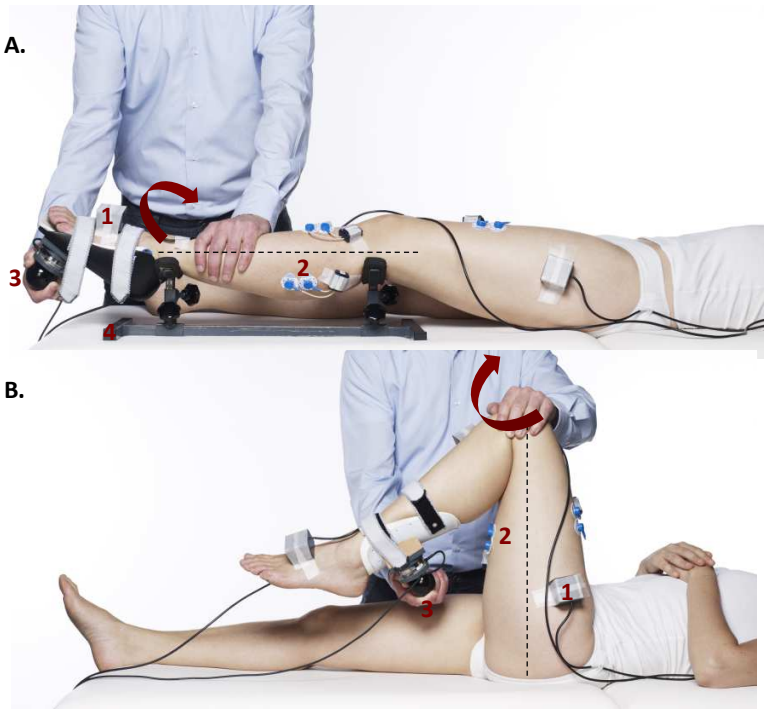

Figure 2

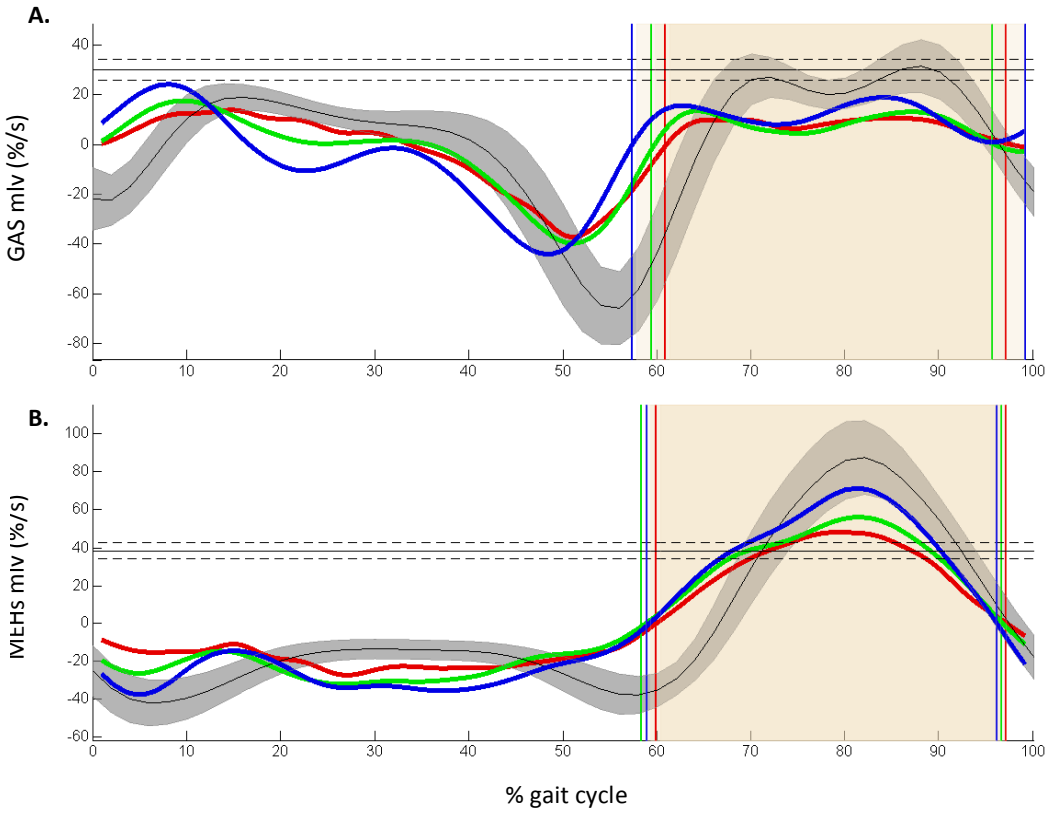
A.
GAS mIv (%/s)
40
20
0
-20
-40
-60
-80
0
10
20
30
40
50
60
70
80
90
100
B.
MEHS mIv (%/s)
100
80
60
40
20
0
-20
-40
-60
0
10
20
30
40
50
60
70
80
90
100
% gait cycle

Figure 3

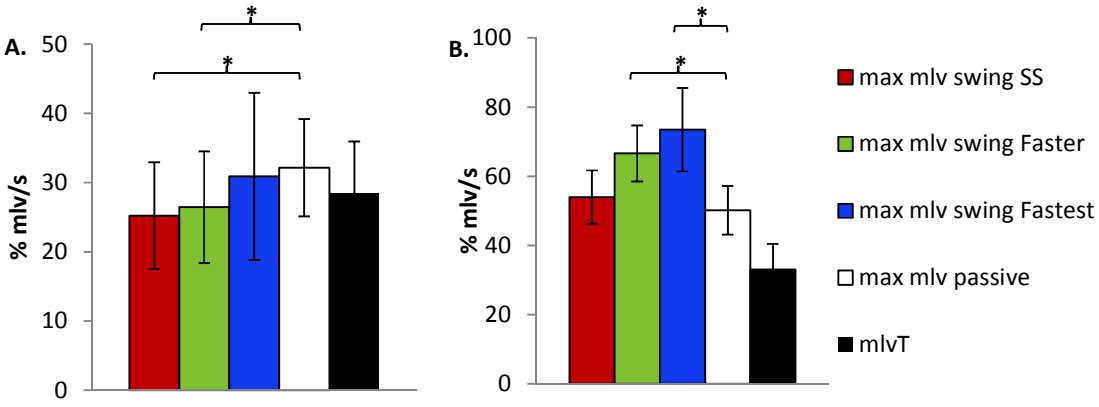
A.
B.
% mlv/s
50
40
30
20
10
0
100
80
60
40
20
0
*
*
max mlv swing SS
max mlv swing Faster
max mlv swing Fastest
max mlv passive
mlvT

Figure 4

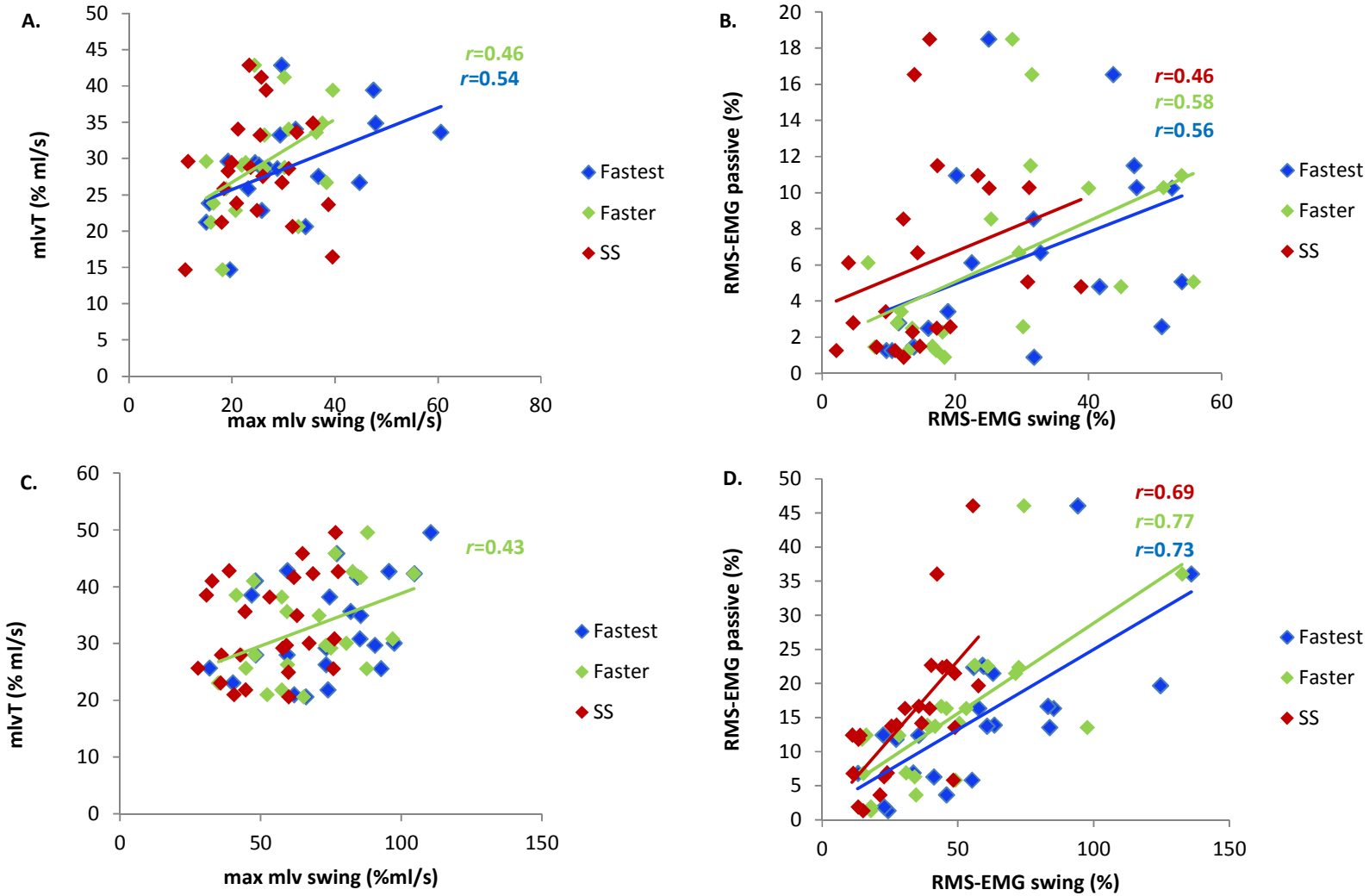
A.
mlvT (% ml/s)
max mlv swing (%ml/s)
r=0.46
r=0.54
Fastest
Faster
SS
B.
RMS-EMG passive (%)
RMS-EMG swing (%)
r=0.46
r=0.58
r=0.56
Fastest
Faster
SS
C.
mlvT (% ml/s)
max mlv swing (%ml/s)
r=0.43
Fastest
Faster
SS
D.
RMS-EMG passive (%)
RMS-EMG swing (%)
r=0.69
r=0.77
r=0.73
Fastest
Faster
SS

Table 1. Subject/muscle characteristics

Subjects	**GAS** (n=22)	**MEHs** (n=24)
Gender m/f	14/8	14/10
Mean age years (SD)	10.2 (3.1)	10.4 (3.3)
Diagnosis	Di: 13; LH: 2; RH: 7	Di: 14; LH: 2; RH: 7; Tri: 1
GMFCS score (I-IV)	I: 12; II: 6; III: 4	I: 12; II: 7; III: 5
MAS score (I-V)	GAS 1: 2; 1+: 8; 2:10; 3: 2	MEH 1: 4; 1+: 10; 2: 8; 3: 2
Average MTS angle (SD)	-11.7° (11.2°)	-79.0° (8.0°)

Table 2

Table 2. Medians (and interquartile ranges) of parameters from ISA and from the 3D gait analysis

		GAS (n=22)	**MEHs** (n=24)
ISA		Median (IQR)	Median (IQR)
max mlv passive (%/sec)		31.7 (8.0)	50.6 (12.2)
mlvT (%/sec)		28.5 (9.8)	30.5 (15.5)
RMS-EMG passive (% of MVC)		4.9 (7.5)	13.8 (13.3)
3D gait analysis	**Velocity condition**		
max mlv swing (%/sec)	SS	25.2 (10.5)	58.5 (25.4)
	Faster	26.3 (15.7)	65.2 (31.4)
	Fastest	29.5 (19.0)	74.2 (27.4)
diff mlv (%/sec)	SS	-3.5 (11.1)	21.5 (18.0)
	Faster	-2.4 (9.7)	35.7 (24.6)
	Fastest	-0.3 (16.0)	44.7 (24.9)
RMS-EMG swing (% of MVC)	SS	14.3 (8.3)	33.0 (24.9)
	Faster	25.3 (18.0)	44.7 (33.3)
	Fastest	25.0 (27.8)	58.3 (33.3)

ISA, instrumented spasticity assessment; GAS, lateral gastrocnemius; MEHs, medial hamstrings; max mlv passive, average maximum lengthening velocity during high velocity passive stretches; RMS-EMG, root mean square electromyography; MVC, maximum voluntary contraction; mlvT, the average mlv at EMG onset during high velocity passive stretches; max mlv swing, maximum muscle lengthening velocity during swing; diff mlv, the difference between max mlv swing and the mlvT (negative values indicate that the max mlv swing was lower than the mlvT); SS, self-selected.

Table 3

Table 3A. Spearman rank correlation coefficients (*r*) between passive assessment parameters and gait analysis parameters at all walking conditions for the gastrocnemius (n=22)

Walking condition	RMS-EMG passive	mlvT	Diff mlv
Self-selected			
max mlv swing	-.03	.07	.65*
RMS-EMG swing	**.46***	-.27	-0.23
Diff mlv	.16	-.66*	1.00
Faster			
max mlv swing	-.23	**.46***	.57*
RMS-EMG swing	**.58***	-.28	-0.22
Diff mlv	.09	-.37	1.00
Fastest			
max mlv swing	-.20	**.54***	.73*
RMS-EMG swing	**.56***	-.05	-0.08
Diff mlv	.06	-.11	1.00

Table 3B. Spearman rank correlation coefficients (*r*) and corresponding p-values (*p*) between passive assessment parameters and gait analysis parameters at all walking conditions for the medial hamstrings (n=24)

Walking condition	RMS-EMG passive	mlvT	Diff mlv
Self-selected			
max mlv swing	-.37	.31	.82*
RMS-EMG swing	**.69***	-.17	-0.45*
Diff mlv	-.38	-.22	1.00
Faster			
max mlv swing	-.29	**.43***	.89*
RMS-EMG swing	**.77***	-.21	-0.41*
Diff mlv	-.27	.03	1.00
Fastest			
max mlv swing	-.30	.39	.90*
RMS-EMG swing	**.73***	-.05	-0.25*
Diff mlv	-.28	.00	1.00

Max mlv swing, maximum muscle lengthening velocity during swing; mlvT, the average mlv at EMG onset during high velocity passive stretches; Diff mlv, the difference between max mlv swing and mlvT; RMS-EMG passive, average root mean square electromyography during high velocity passive stretches; RMS-EMG swing, average RMS-EMG during the lengthening phase of swing; *$p<0.05$; significant correlations between passive assessment parameters and gait analysis parameters appear in **bold**.

Appendix

Table 1. Results from an intra-rater reliability study (Bar-On, Aertbeliën, Molenaers, & Desloovere, 2014) of instrumented spasticity parameters in 10 children with spastic CP (11.9yrs ± 3.8yrs).

Parameter	Test mean (SD)	Re-test mean (SD)	ICC	SEM
Lateral gastrocnemius				
max mlv passive (%/s)	31.78 (5.67)	30.96 (4.83)	0.93	2.02
mlvT (%/s)	27.16 (5.97)	28.01 (4.99)	0.80	2.50
RMS-EMG passive (%)	7.65 (5.25)	5.71 (4.78)	0.78	2.89
Medial hamstrings				
max mlv passive (%/s)	37.77 (10.90)	39.16 (8.67)	0.86	3.69
mlvT (%/s)	25.30 (12.34)	28.45 (7.25)	0.78	6.02
RMS-EMG passive (%)	16.93 (7.77)	16.87 (7.90)	0.79	4.85

Max mlv passive, average maximum lengthening velocity during high velocity passive stretches; mlvT, muscle lengthening velocity reflex threshold; RMS-EMG passive, root mean square electromyography collected during tests in a passive muscle.

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